COLLAGEN REPLACEMENT PROTHESIS FOR THE CORNEA

This is a division of application Ser. No. 431,578 filed Sept. 30, 1982, now U.S. Pat. No. 4,505,855.

FIELD OF THE INVENTION

This invention relates to a prosthetic replacement for the cornea and particularly to a transparent collagen material useful for making such a prosthesis and to methods for making such transparent collagen material.

BACKGROUND OF THE INVENTION

Most synthetic polymer membranes are extruded from the cornea after intralamellar implantation. This is explained by their impermeability, both to water and metabolites, which causes desiccation of the corneal stroma anterior to the membrane. It has been suggested that an approach to the problem of finding a suitable corneal implant material is the use of collagen.

Collagen is a protein which constitutes about 20 to 30 percent of the total body protein in vertebrates. It is a fibrous protein and functions primarily as a supporting tissue and scaffolding for other proteins and cells. It is present throughout the body but exists in high concentrations in skin, tendon and bone.

Collagen is recovered from these tissues by a variety of techniques, the oldest known method being the boiling of the tissue in water which denatures some of the collagen and forms gelatin on cooling. For use as a biomaterial however, collagen must be recovered in native, undenatured form, i.e., with little or no destruction of the basic rigid triple helical structure (tropocollagen).

Undenatured native collagen is recovered principally by two methods, (a) solution by dissolving the collagen in acids, bases, salts or by enzyme digestion, in which instances the collagen becomes actually dissolved, and (b) extraction in solid, undissolved, fiber form (hereinafter "fibrous collagen) usually by the action of aqueous salt or minced, comminuted collagen raw material to produce a dispersion from which the solid is recovered by centrifugation, etc. Both the solution and extraction methods are described in the collagen art.

Collagen materials have been studied for many years and for many suggested uses. For example, Dunn et al, in *Science,* 157 pp. 1329–30 (1967), the disclosure of which is incorporated herein by reference, describe the use of collagen-derived membranes for corneal implantation. Dunn et al, in *Ophthalmic Surg.,* 2(1), pp. 9–11 (1971), the disclosure of which is incorporated herein by reference, described the use of collagen membranes for intralamellar corneal implants in experimental surgery. U.S. Pat. No. 4,268,131, the disclosure of which is incorporated herein by reference, describes a soft contact lens made from fibrous collagen and mixtures of such fiber with purified solubilized collagen. U.S. Pat. No. 4,223,984, the disclosure of which is incorporated herein by reference, describes soft contact lenses made from solubilized, defatted, cross-linked collagen, and/or chemically modified collagen. U.S. Pat. No. 4,164,559 describes a chemically modified membrane as a carrier for ophthalmic medication leaving no removable material after drug release. U.S. Pat. No. 4,233,360 describes a method for preparing non-mitigenic collagen and suggests its use for medical products such as sponges, prosthetic devices, films, membranes, sutures, etc. U.S. Pat. No. 4,279,812 describes a method for preparing macromolecular biologically active collagen and suggests its use for making implants for slow release of medication. See also Dunn et al., "Corneal Derived Membrane: Corneal Implantations," in *Biomaterials,* edited by Stark and Agarwal, Plenum Press, New York (1969) at pp. 195–199, the disclosure of which is incorporated herein by reference.

To date, no one to the knowledge of the present applicants has successfully produced a collagen material that can be used as a prosthetic replacement for the cornea. Typically collagen materials, although transparent when used in thin membranes, are not sufficiently transparent when made in a thickness suitable for use as a prosthetic replacement for the cornea.

Thus, there remains a desire for a native collagen material suitable for making a prosthetic replacement for the cornea.

SUMMARY OF THE INVENTION

The present invention provides a transparent native, non-fibrilized collagen material having an absorbance at a wavelength 900 nm of less than 5% in a sample 5 mm thick. This collagen material of the present invention is useful for prosthetic replacement of the cornea because of the high transparency and because it is a native material, and thus less susceptible to immunogenic responses.

The collagen material is preferably made by ultracentrifuging a cold collagen solution, i.e., centrifuging at about 80,000 or more times gravity, preferably at about 100,000–120,000 times gravity until the level of supernate is constant. The supernate is removed and the pellet is fixed by treating it to produce cross-linking between the molecules of collagen.

The collagen material of this invention can also be used for prosthetic replacement of other bodily tissues, such as nucleus pulposus, cartilage, and vitreous body.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a graph of absorbance versus wavelength for a 5 mm thick sample of the collagen material of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Prior to the present invention the use of collagen based materials in cases where transparency is important has been limited to use as thin membranes, because prior art collagen materials were not sufficiently transparent for optical use except in such membrane from where the thinness made up for the lack of transparency.

The collagen material of the present invention, however, is a highly transparent, relatively hard non-fibrilized gel, and thus it is advantageous for use in corneal replacement. The collagen material of this invention is made from soluble native collagen. Preferably the collagen is first extracted from native materials such as skin, rat tail tendons, or tendons from other parts of mammals, by dissolution. As noted above, the method can involve dissolution in acids, bases, salts, or enzymatic dissolution. Preferably the collagen is derived by acidic dissolution of the natural source, e.g., by dissolution of rat tail tendon in acetic acid. Although the acid extract is commonly referred to as a "solution", its exact molecular make-up is not precisely known, and the molecular weight of collagen (usually about 300,000) is such that "solutions" of it may also have some properties usually